# BEST AVAILABLE COOV

| PT() 1542<br>(4 85)  |                                       |   | U.S. DEPARTMENT OF COMMER PATENT AND TRADEMARK OFF |
|--|---------------------------------------|---|--|
| ON   | LINE SEARCH REQUE                     | ST FORM                                       |  |
| **************************************   | * * * * * * * * * * * * * * * * * * * | 6773 <b>00</b>                                | **********   |
| ART UNIT PH  | 308-3453                              |   | 1 121193   |
| Please give a detailed statemen<br>matter to be searched. Define ar<br>citations, authors, or keywords, if | ny terms that may have sp             | e as specifically as<br>ecial meaning. Give ( | possible the subject examples orant                |
| You may include a copy of the bro  | padest and or relevant claim          | (s).  |  |
| Please search  | SEQ 10 A                              | 14<br>10; <b>15</b>                           | n⇔4 amino acid                                     |
|  |                                       |   |  |
| sequence against pro   | tein data bases inclu                 | ding GeneSeqRe                                | versuctranstate the                                |
| -highlighted partions  | Search against n                      | NOS 13<br>ucleic acid data                    | bases including                                    |
|  | 4 .                                   |   |  |
| GeneSeq.   |                                       |   |  |
| DO NOT PRINT T   | HE SEARCHES, but save                 | ALL to a SINGLE                               | COMBINED file on the                               |
| attached diskette.   |                                       |   | ×2*  |
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| EEQ B. (ES)  | ,                                     |   |  |
| , KER II LES !   | -1 -                                  |   |  |
| SFQ (C)  |                                       |   |  |
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| •  |                                       |   | 1-161  |
|  | v                                     |   |  |
| *  | ******                                | * * * * * * * * *                             | ******   |
|  | STAFF USE ONLY                        |   | • •  |
| COMPLETED WALL XILOUX  | <del></del>                           | SYSTEMS ——— CAS ON                            |  |
| SEARCHER   | 17                                    | DIALOG  | DUESTEL  |
| NO. OF DATABASES   | · · · · · · · · · · · · · · · · · · · | SDC OTHER                                     | 6  |
| 2. 12. tan   |                                       | `   |  |

> 0 ( Ol 10 IntelliGenetics > 0 ( FastDB - Fast Pairwise Comparison of Sequences Release 5.4 Results file us-07-800-364a-13.res made by maryh on Thu 21 Jan 93 19:51:42-PST. Query sequence being compared: US-07-800-364A-13 (1-1003) Number of sequences searched: 131368 Number of scores above cutoff: 4260 Results of the initial comparison of US-07-800-364A-13 (1-1003) with: Data bank : EMBL-NEW 12, all entries Data bank : GenBank 74, all entries Data bank : GenBank-NEW 12, all entries Data bank : N-GeneSeq 9, all entries Data bank: UEMBL 33 74, all entries 4. US-07-800-364A-13 (1-1003) HUMOP1 Human OP-1 mRNA for osteogenic protein HUMOP1 LOCUS 1878 bp ss-mRNA PRI 29-MAY-1991 DEFINITION Human OP-1 mRNA for osteogenic protein ACCESSION X51801 KEYWORDS OP-1 gene; osteogenic protein. SOURCE Homo sapiens RNA. ORGANISM Homo sapiens Eukaryota; Animalia; Chordata; Vertebrata; Mammalia; Theria; Eutheria; Primates; Haplorhini; Catarrhini; Hominidae. REFERENCE (bases 1 to 1878) AUTHORS Oppermann, H. JOURNAL Unpublished (1990) STANDARD full automatic REFERENCE 2 (bases 1 to 1878) AUTHORS Oezkaynak, E., Rueger, D.C., Drier, E.A., Corbett, C., Ridge, R.J., Sampath, T.K. and Oppermann, H. TITLE OP-1 cDNA encodes an osteogenic protein in the TGF-beta family JOURNAL EMBO J. 9, 2085-2093 (1990) STANDARD full automatic COMMENT \*source: tissue=placenta; entry HSOP1; dated 12-SEP-1990. From EMBL **FEATURES** Location/Qualifiers polyA\_signal 1850..1855 /gene="BMP3"

ي زيدر م

يه رواحة من

1862..1867

polyA\_signal

/translation="MHVRSLRAAAPHSFVALWAPLFLLRSALADFSLDNEVHSSFIHR RLRSQERREMQREILSILGLPHRPRPHLQGKHNSAPMFMLDLYNAMAVEEGGGPGGQG FSYPYKAVFSTQGPPLASLQDSHFLTDADMVMSFVNLVEHDKEFFHPRYHHREFRFDL SKIPEGEAVTAAEFRIYKDYIRERFDNETFRISVYQVLQEHLGRESDLFLLDSRTLWA SEEGWLVFDITATSNHWVVNPRHNLGLQLSVETLDGQSINPKLAGLIGRHGPQNKQPF MVAFFKATEVHFRSIRSTGSKQRSQNRSKTPKNQEALRMANVAENSSSDQRQACKKHE

LYVSFRDLGWQDWIIAPEGYAAYYCEGECAFPLNSYMNATNHAIVQTLVHFINPETVP

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FRISVYQVLQEHLGRESDLFLLDSRTLWASEEGWLVFDITATSNHWVVNPRHNLGLQL

SVETLDGQSINPKLAGLIGRHGPQNKQPFMVAFFKATEVHFRSIRSTGSKQRSQNRS"

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### MVMSFVNLVEHDKEFFHPRYHHREFRFDLSKIPEGEAVTAAEFRIYKDYIRERFDNET

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FRISVYQVLQEHLGRESDLFLLDSRTLWASEEGWLVFDITATSNHWVVNPRHNLGLQL
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QDWI I APEGYAAYYCEGECAFPLNSYMNATNHA I VQTLVHF I NPETVPKPCCAPTQLN
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BASE COUNT
               411 a
                       592 c
                              541 g
                                      334 t
ORIGIN
Initial Score
                   513 Optimized Score
                                           630 Significance = 30.73
                   64%
                       Matches
                                           670 Mismatches
                                                              303
Residue Identity =
                                                                0
Gaps
                    59
                       Conservative Substitutions
                              20
                                       30
                                               40
                                                        50
                                                                 60
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            X
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                                                              620
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                   80
                            90
                                    100
                                                 110
                                                           120
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    11 11 1 111
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       630
                640
                         650
                                    660
                                              670
                                                      680
                                                               690
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                      150
                               160
                                       170
                                                180
                                                         190
   CCACGTCAGCATGTTCCAGGTGGTCCAGGAGCAGTCCAACAGGGAGTCTGACTTGTTCTTTTTGGATCTTCA
        111111 11 11 1 111 1 1 11
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|                       | 700                                | 710                                       | 720                                     | 730  | 740                                      | 750                                      | 760                                      |
|-----------------------|------------------------------------|---|---|--|--|--|--|
| II<br>TACCI           | 111 1 11                           | 11 1111                                   | 111111111                               | 240<br>GCTGGATGTCA<br>IIIIIII<br>GTTTGACATCA<br>800      | 1111 1111                                |  | 1  11  1  11                             |
| 1                     | II IIII<br>CGGCACA                 | GACCTGGGAC                                | 1111                                    | TGTGGAGACTO<br>         <br>GGTGGAGACGO                  |  |  | TCCTGGCCT                                |
|                       | IIIIII I<br>GCCTGATT               | III III<br>GGGCGGCACG                     | IIIIIII I<br>3GCCCCA-GA                 | 380<br>TCCCAACAGCO<br>I IIIIII<br>AC-AAGCAGCO<br>940     | 111 1111                                 | 11111111                                 | CAGGGCCAGT                               |
| 1 11                  | 1111 1 1                           | IIIII I<br>CCGCAGCATC                     | III I I<br>CGGTCCACGG                   | GGCCACTGAGG  | 11 1111                                  | н нн                                     | AGCAACGAGC<br>II III<br>CGCTCCAAGA       |
| 111                   | GCAGGCCAA                          | I II<br>GGAAGCCCTG                        | 1111                                    | 520<br>TGATGAC-GTO<br>IIII<br>ACGTGGCAGAG<br>1080        | CACGGCTCCC                               | CACGGCC                                  | 111111 11                                |
| 1                     | TCGGCACGA                          | GCTCTACGTC<br>                            | AGCTTCCAGG<br>        <br> AGCTTCCGAG   | 80 59<br>ACCTTGGCTGG<br>           <br>ACCTGGGCTGG       | GCTGGACTGGG<br>          <br>GCAGGACTGGA | TCATCGCCC                                | 1 111111                                 |
| ACTCA<br>II I<br>ACGC | AGCCTATTA<br>IIIII II<br>CGCCTACTA | CTGTGAGGGG<br>             <br>CTGTGAGGGG | SAGTGCTCCT<br>           <br>SAGTGTGCCT | 660<br>TCCCGCTGGAC<br>IIII III II<br>TCCCTCTGAAC<br>1220 | TCCTGCATGA<br>                           | AACGCCACCA<br>IIIIIIIIIIII<br>AACGCCACCA | AACCACGCCA<br>           <br> AACCACGCCA |
| TCCT                  | SCAGTCCCT<br>                      | GGTGCACCTG<br>             <br>GGTCCACTTC | ATGAAGCC<br>II II II<br>ATCAACCCGG      | 730<br>AAACGCAGTCC<br>IIIII II I<br>AAACGGTGC<br>290     | CCAAGGCGTO                               | CTGTGCACC                                | CACCAAGCT                                |

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760
           770
                     780
                               790
                                        800
                                                  810
                                                            820
                                                                      830
   GAGCGCCACCTCTGTGCTCTACTATGACAGCAGCAACACGTCATCCTGCGCAAGCACCGCAACATGGTGGT
      CAATGCCATCTCCGTCCTCTACTTCGATGACAGCTCCAACGTCATCCTGAAGAAATACAGAAACATGGTGGT
     1330
               1340
                         1350
                                   1360
                                            1370
                                                      1.380
                                                                1390
                                                                       900
         840
                   850
                                                   880
                                                             890
                             860
                                          870
   CAAGGCCTGCGGCTGCCACTGAGTCAGCC---CGCCCAGCCCTACTGCAGCCACCCTTCTCATCTGGATCGG
     11 11
                                       111 11
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                                                   1111
                                                          11
   CCGGGCCTGTGGCTGCCACTAGCTCCTCCGAGAATTCAGACCCTTTGGGGCCAAGTTT---TTCTGGATCCT
    1400
             1410
                       1420
                                 1430
                                          1440
                                                    1450
                                                                 1460
          910
                    920
                              930
                                        940
                                                 950
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                                                                     970
   GCCCTGCAGAGGCAGAAAACCCTTAAATGCTGTCACAGCTCAAGCAGGAGTGTCAGGGGCCCTCACTCTCGG
              11
                      1
                               11 1 1 11 11
                                                 11111 11 11
                           1
   CCATTGC--TCGCCTTGGCCAGGACCAGCAGAC-CAACTGCCTTTTGTGAGAC-CTTCCCCTCCCTATCCC
    1470
                1480
                          1490
                                    1500
                                              1510
                                                         1520
                                                                   1530
        980
                     990
                              1000 X
   TGCCTACTT---CCTGTCAGGCTTCTGGGAATTC
      11 11
                 CAACT--TTAAAGGTGTGAGAGTATTAGGAAACATGAGCAGCAT
                            1560
                                    X 1570
        1540
                  1550
7. US-07-800-364A-13 (1-1003)
  HUMTGFBD
               Human transforming growth factor-beta (tgf-beta) m
LOCUS
                         1448 bp ss-mRNA
                                                   PRI
                                                             15-JAN-1991
            HUMTGFBD
            Human transforming growth factor-beta (tgf-beta) mRNA, complete
DEFINITION
            cds.
ACCESSION
            M60316 M38693 M38695
KEYWORDS
            transforming growth factor-beta.
SOURCE
            Human cell line U-2 OS, cDNA to mRNA.
  ORGANISM
            Homo sapiens
            Eukaryota; Animalia; Chordata; Vertebrata; Mammalia; Theria;
            Eutheria: Primates: Haplorhini: Catarrhini: Hominidae.
REFERENCE
               (bases 1 to 1448)
            Celeste, A.J., Iannazzi, J.A., Taylor, R.C., Hewick, R.M., Rosen, V.,
  AUTHORS
            Wang, E.A. and Wozney, J.M.
  TITLE
            Identification of new tgf-beta family members present in
            bone-inductive protein purified from bovine bone
  JOURNAL
            Proc. Natl. Acad. Sci. U.S.A. 87, 9843-9847 (1990)
  STANDARD
            full automatic
FEATURES
                     Location/Qualifiers
     CDS
                     97..1392
                     /gene="tgf-beta"
                     /product="transforming growth factor-beta"
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/codon\_start=1

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| 111 111  | III I II I<br>CTGATTGGGCGG | 11111111      | 11 1 1                                   | 11111 111                                  |                                      | 400<br>CTTCAGGGCCAGT<br>IIIII IIIII<br>CTTCAAGGCCA<br>940           |
|          | 11 1 111111                | 1 111 1       | 1 11 1                                   | 1 11                                       |                                      | ACCGCTCCAAGA  |
| 111 11   | GGCCAACCGACT<br>           | 11 1111       | I II<br>GGCCAACGTGG                      |  | 1 11 11                              | 540<br>CGGCAGGTCT<br>I IIIIII II<br>CAGAGGCAGGCCT<br>1080           |
| 1        |                            | 11111111      | 11 11111 1                               | 111111 111                                 | 1111 111111                          | 610<br>GCCCCCAAGGCT<br>II II IIIIII<br>GCGCCTGAAGGCT<br>1150        |
| 11 1 111 |                            | 111111111     | 111111111111111111111111111111111111111  | 11 111111                                  |                                      | 680<br>ACCAACCACGCCA<br>             <br>ACCAACCACGCCA<br>  220     |
| 11 11111 | STCCCTGGTGCA               | CCTGATGAA<br> | 11 11111                                 | 11 111111                                  | 1 11111111                           | 750<br>CACCCACCAAGCT<br>IIIII IIII<br>CGCCCACGCAGCT<br>1290         |
| 1 1111   | ACCTCTGTGCTC               | TACTATGAC     | AGCAGCAACAA(<br>IIII III<br>GACAGCTCCAA( | CGTCATCCTG(<br>           <br> CGTCATCCTG( | II II<br>AAGAAATACAG                 | 20 830<br>GCAACATGGTGGT<br>FILLILITITI<br>GAAACATGGTGGT<br>860 1370 |
| CCGGGCCT | GCGGCTGCCAC                | TGAGTCAGC     | CCGCCCAG(                                | CCCTACTGCAG                                | SCCACCCTTC1<br>       <br> SCCAAGTTT | 390 900<br>CCATCTGGATCGG<br>IIIIIIII<br>TTCTGGATCCT                 |

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1 111
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 1440
           Χ
8. US-07-800-364A-13 (1-1003)
   MUSOP1G
                Mouse OP-1 mRNA for osteogenic protein 1
LOCUS
                          1872 bp ss-mRNA
                                                     ROD
                                                               10-OCT-1991
            MUSOP16
 DEFINITION Mouse OP-1 mRNA for osteogenic protein 1
 ACCESSION
             X569@6
 KEYWORDS
             OP-1 gene; osteogenic protein.
            Mus musculus RNA.
 SOURCE
  ORGANISM Mus musculus
             Eukaryota; Animalia; Chordata; Vertebrata; Mammalia; Theria;
             Eutheria; Rodentia; Myomorpha; Muridae; Murinae.
                (bases 1 to 1872)
 REFERENCE
             Ozkaynak, E., Schnegelsberg, P.N. and Oppermann, H.
  AUTHORS
            Murine osteogenic protein (OP-1): High levels of mRNA in kidney
   TITLE
   JOURNAL
            Biochem. Biophys. Res. Commun. 179, 116-123 (1991)
  STANDARD full automatic
 COMMENT
             Sequenced molecule was a DNA/cDNA composite:- genomic clone bases
             1-465, cDNA clone bases 267-1872.
                From EMBL
                             entry MMOP1G; dated 26-SEP-1991.
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EEGWLVFDITATSNHWVVNPRHNLGLQLSVETLDGQSINPKLAGLIGRHGPQNKQPFM
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### PCCAPTQLNAISVLYFDDSSNVILKKYRNMVVRACGCH" BASE COUNT 433 a 591 c 501 q 347 t ORIGIN Optimized Score = Initial Score 637 Significance = 29.20 65% Matches Mismatches Residue Identity = Gaps Conservative Substitutions 1 1 1111 1 AGAATTCTTCCACCCTCGATACCACCATCG---GGAGTTCCGGTTTGATCTTTCCAAGATCCCCGAGGGCGA 540 X GGCGGTCACAGCTGCGGAGTTCCGGATTTACAAGG--TGC--CCAGCATCCACCTGCTCAACAGGACCCTCC ACGGGTGACCGCAGCCGAATTCAGGATCTATAAGGACTACATCCGGGAGCGATTTG-ACAACGAGACCTTCC ACGTCAGCATGTTCCAGGTGGTCCAGGAGCAGTCCAACAGGGAGTCTGACTTGTTCTTTTTTGGATCTTCAGA 1 1 CGCTCCGAGCTGGAGACGAGGGCTGGCTGGTGCTGGATGTCACAGCCAGTGACTGCTGGTTGCTGAAGC CCATCTGGGCTTCTGAGGAGGGCTGGTTGGTGTTTGATATCACAGCCACCAGCAACCACTGGGTGGTCAACC GTCACAAGGACCTGGGACTCCGCCTCTATGTGGAGACTGAGGATGGGCACAGCGTGGATCCTGGCCTGGCCG CTCGGCACAACCTGGGCTTACAGCTCTCTGTGGAGACCCTGGATGGGCAGAGCATCAACCCCAAGTTGGCAG GCCTGCTGGGTC--AACGGGCCCCACGCTCCCAACAGCCTTTCGTGGTCACTTTCTTCAGGGCCAGTCCG-A GCCTGATTGGACGGCATGGACCCCA-GAAC-AAGCAACCCTTCATGGTGGCCTTCTTCAAGGCCA--CGGAA GTCC-CATCCGCACCCTCGG-GCAGTGAGGCCACTGAGGAGGAGGCAGCCGAAGAAAAGCAACGAGCTGCC 111 11 11111 11 11 313131 1111 11 111 111 GTCCATCTCCGTAGTATCCGGTCCACGGGGGGCA---AGCAG--CGCAGCC--AGAATCGCTCCAAGACGCC

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              1190
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           11 11 1
                           11111 1111 11 1
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                                        1450
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          920
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                          950
                                960
                                      970
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                111 1 11 11
      1 11 1 11 1
                         1 11
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                                1500
      1460
                    1480
                           1490
                                      1510
   980
          990
                1000 X
  CCTACTTCCTGTC--AGGCTTCTGG--GAATTC
  CCTTC-CCCTCACCTCCCCAACCGGAAGCATGTAAGGGTTCCA
    1520
          1530
               1540
) 0 (
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Ol IO IntelliGenetics

### ) 0 (

FastDB - Fast Pairwise Comparison of Sequences Release 5.4

Results file us-07-800-364a-14-pir.res made by maryh on Thu 21 Jan 93 19:33:50-PST.

Query sequence being compared:US-07-800-364A-14 (1-281)
Number of sequences searched: 44900
Number of scores above cutoff: 4198

Results of the initial comparison of US-07-800-364A-14 (1-281) with: Data bank : PIR 34, all entries

|     |        | **** 53 standard deviations above | e mean  | **** |     |       |   |
|-----|--------|-----------------------------------|---------|------|-----|-------|---|
| 1.  | S10529 | *Osteogenic protein precursor     | 431     | 132  | 158 | 53.25 | 0 |
| 2.  | C39263 | *Bone morphogenetic protein 7     |         | 132  | 158 | 53.25 | 0 |
|     |        | **** 51 standard deviations above |         |      |     |       | _ |
| 3.  | JQ1184 | Osteogenic protein 1 precurso     |         | 132  | 155 | 51.86 | 0 |
|     |        | **** 50 standard deviations above | e mean  | **** |     |       |   |
| 4.  | A39263 | *Bone morphogenetic protein 5     | 454     | 111  | 153 | 50.93 | 0 |
| 5.  | A33925 | *Vg-1-related protein precurs     | 438     | 128  | 152 | 50.47 | Ø |
| 6.  | B39263 | *Bone morphogenetic protein 6     |         | 128  | 151 | 50.01 | 0 |
|     |        | **** 25 standard deviations above |         |      |     |       |   |
| 7.  | A41233 | Bone morphogenetic protein ho     | 455     | 63   | 99  | 25.93 | 0 |
|     |        | **** 21 standard deviations above | e mean  | **** |     |       |   |
| 8.  | A26158 | Decapentaplegic protein precu     | 588     | 54   | 89  | 21.30 | 0 |
|     |        | **** 19 standard deviations above | ve mean | ***  |     |       |   |
| 9.  | C37278 | Bone morphogenetic protein 2B     | 408     | 36   | 86  | 19.91 | 0 |
|     |        | **** 18 standard deviations above | ve mean | **** |     |       |   |
| 10. | C39364 | *GDF-1 embryonic growth facto     | 372     | 28   | 83  | 18.52 | 0 |
| 11. | A29619 | Vg1 embryonic growth factor -     | 360     | 55   | 82  | 18.06 | Ø |
|     |        | **** 17 standard deviations above | e mean  | ***  |     |       |   |
| 12. | B37278 | Bone morphogenetic protein 2A     | 396     | 35   | 81  | 17.59 | Ø |
|     |        | **** 16 standard deviations above | e mean  | **** |     |       |   |
| 13. | S16244 | Bone morphogenetic protein 2      | 398     | 35   | 78  | 16.21 | 0 |
|     |        | **** 14 standard deviations above | e mean  | **** |     |       |   |
| 14. | A30884 | Inhibin beta-A chain precurso     | 426     | 20   | 74  | 14.35 | Ø |
| 15. | B24248 | Inhibin beta-A chain precurso     | 426     | 20   | 74  | 14.35 | 0 |
| 16. | A39364 | *GDF-1 embryonic growth facto     | 357     | 20   | 74  | 14.35 | Ø |
| 17. | A35683 | *GDF-1 embryonic growth facto     | 357     | 20   | 74  | 14.35 | 0 |
|     |        | **** 13 standard deviations above | e mean  | ***  |     |       |   |
| 18. | WFPGBA | Inhibin beta-A chain precurso     | 424     | 20   | 73  | 13.89 | 0 |
|     |        | **** 12 standard deviations above | e mean  | **** |     |       |   |
| 19. | B40905 | *Inhibin beta-A chain precurs     | 424     | 20   | 71  | 12.96 | 0 |
| 20. | B40056 | *Inhibin beta-A chain precurs     | 424     | 20   | 71  | 12.96 | Ø |
|     |        |                                   |         |      |     |       |   |

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1. US-07-800-364A-14 (1-281)
               *Osteogenic protein precursor - Human
  S10529
ENTRY
                          #Type Protein
                *Osteogenic protein precursor - Human
TITLE
                15-Jun-1992 #Sequence 15-Jun-1992 #Text 15-Jun-1992
DATE
PLACEMENT
                   0.0
                         0.0
                                0.0
                                      0.0
                                             0.0
COMMENT
                *This entry is not verified.
                Homo sapiens #Common-name man
SOURCE
REFERENCE
                Oezkaynak E., Rueger D.C., Drier E.A., Corbett C.,
   #Authors
                  Ridge R.J., Sampath T.K., Oppermann H.
   #Journal
                EMBO J. (1990) 9:2085-2093
   #Title
                OP-1 cDNA encodes an osteogenic protein in the
                  TGF-beta family.
   #Reference-number S10529
                S10529
   #Accession
   #Cross-reference EMBL:X51801
              #Molecular-weight 49313 #Length 431 #Checksum
                                                             128
SUMMARY
SEQUENCE
                                              158 Significance = 53.25
Initial Score
                    132 Optimized Score =
                    56% Matches
                                              161 Mismatches
                                                                   115
Residue Identity =
Gaps
                     11 Conservative Substitutions
                                                                     Ø
                                                  40
                                                            50
                     10
                              20
                                        30
             EPHWKEFRFDLTQIPAGEAVTAAEFRIYK-VPSIHLLNRTLHVSMFQVVQEQSNRESDLFFL
                                                1 1 1 11 11
               VEHDKEFFHPRYHHREFRFDLSKIPEGEAVTAAEFRIYKDYIRERFDNETFRISVYQVLQEHLGRESDLFLL
                                                                    210
  140
                    160
                              170
                                       180
                                                 190
                                                          200
           150
          70
                                      100
                                               110
                                                         120
                                                                  130
                   80
                             90
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      DSRTLWASEEGWLVFDITATSNHWVVNPRHNLGLQLSVETLDGQSINPKLAGLIGRHGPQNKQPFMVAFFKA
         220
                   230
                            240
                                     250
                                               260
                                                         270
                                                                  280
                                                            190
                                                                     200
                 150
                               160
                                         170
                                                  180
       140
   SPSPIRTPRAVRPLRRRQ----PKKSNELPQANRLPGIFDDVHGSHGRQVCRRHELYVSFQDLGWLDWVIA
                                              1 11 1 1111111 1111 11 11
                 1 1
                         11
                              1 11
   TEVHFRSIRSTGSKQRSQNRSKTPKNQEALRMAN-----VAENSSSDQRQACKKHELYVSFRDLGWQDWIIA
                                                  330
                                                            340
       290
                 300
                          310
                                        320
                                       240
                                                250
                                                          260
                                                                   270
          210
                   220
                             230
   PQGYSAYYCEGECSFPLDSCMNATNHAILQSLVHLMKPNAVPKACCAPTKLSATSVLYYDSSNNVILRKHRN
                                      1 111 11111 1 1 1111 1 1 1111 1 11
    PEGYAAYYCEGECAFPLNSYMNATNHAIVQTLVHFINPETVPKPCCAPTQLNAISVLYFDDSSNVILKKYRN
                   370
                             380
                                       390
                                                400
                                                          410
                                                                   420
          360
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Χ

MVVKACGCH III IIIII MVVRACGCH 430

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2. US-07-800-364A-14 (1-281)
  C39263
                *Bone morphogenetic protein 7 - Human
ENTRY
                C39263
                           #Type Protein
 TITLE
                *Bone morphogenetic protein 7 - Human
DATE
                04-Oct-1991 #Sequence 04-Oct-1991 #Text 04-Oct-1991
 PLACEMENT
                   0.0
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                                 0.0
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COMMENT
                 *This entry is not verified.
SOURCE
                Homo sapiens #Common-name man
 REFERENCE
   #Authors
                Celeste A.J., Iannazzi J.A., Taylor R.C., Hewick
                   R.M., Rosen V., Wang E.A., Wozney J.M.
   #Journal
                Proc. Natl. Acad. Sci. U.S.A. (1990) 87:9843-9847
   #Title
                 Identification of transforming growth factor beta
                   family members present in bone-inductive protein
                   purified from bovine bone.
   #Reference-number A39263
   #Accession
                039263
   #Cross-reference GB:M38695
              #Molecular-weight 49313 #Length 431 #Checksum
SUMMARY
                                                                128
SEQUENCE
Initial Score
                     132 Optimized Score =
                                                158 Significance = 53.25
Residue Identity =
                     56% Matches
                                                161 Mismatches
                                                                  =
                                                                      115
Gaps
                      11 Conservative Substitutions
                                                                        0
                     10
                               20
                                          30
                                                    40
                                                              50
                                                                        60
             EPHWKEFRFDLTQIPAGEAVTAAEFRIYK-VPSIHLLNRTLHVSMFQVVQEQSNRESDLFFL
                1 111111 11 1111111111111
                                                  1 1
                                                      1 11 11
                                                                   1111111
   VEHDKEFFHPRYHHREFRFDLSKIPEGEAVTAAEFRIYKDYIRERFDNETFRISVYQVLQEHLGRESDLFLL
  140
           150
                     160
                               170
                                         180
                                                   190
                                                             200
                                                                       210
          70
                                       100
                    80
                              90
                                                 110
                                                           120
                                                                     130
   DLQTLRAGDEGWLVLDVTAASDCWLLKRHKDLGLRLYVETEDGHSVDPGLAGLLGQRAPRSQQPFVVTFFRA
   1 11 1 11111 1 11 1
                                 DSRTLWASEEGWLVFDITATSNHWVVNPRHNLGLQLSVETLDGQSINPKLAGLIGRHGPQNKQPFMVAFFKA
         220
                   230
                             240
                                       250
                                                 260
                                                           270
                                                                     280
                                                              190
                                                                        200
       140
                 150
                                160
                                          170
                                                    180
   SPSPIRTPRAVRPLRRRQ----PKKSNELPQANRLPGIFDDVHGSHGRQVCRRHELYVSFQDLGWLDWVIA
                  1 1
                          11
                                1 11
                                                1 11 1 111111 1111 11 11
   TEVHFRSIRSTGSKQRSQNRSKTPKNQEALRMAN----VAENSSSDQRQACKKHELYVSFRDLGWQDWIIA
                 300
                                                                        350
       290
                           310
                                          320
                                                    330
                                                              340
```

```
220
                                       240
                                                 250
                                                           260
                                                                     270
          210
                              230
   PQGYSAYYCEGECSFPLDSCMNATNHAILQSLVHLMKPNAVPKACCAPTKLSATSVLYYDSSNNVILRKHRN
   PEGYAAYYCEGECAFPLNSYMNATNHAIVQTLVHFINPETVPKPCCAPTQLNAISVLYFDDSSNVILKKYRN
                                                 400
                    370
                              380
                                       390
                                                           410
                                                                     420
          360
   MVVKACGCH
   111 11111
   MVVRACGCH
        430
1. US-07-800-364A-14 (1-281)
  BMP7 HUMAN BONE MORPHOGENETIC PROTEIN 7 PRECURSOR (BMP-7) (OS
     BMP7 HUMAN
ID
                    STANDARD;
                                  PRT;
                                         431 AA.
AC
     F18075:
     01-NOV-1990 (REL. 16, CREATED)
DT
     01-NOV-1990 (REL. 16, LAST SEQUENCE UPDATE)
DT
     01-AUG-1992 (REL. 23, LAST ANNOTATION UPDATE)
DT
DE
     BONE MORPHOGENETIC PROTEIN 7 PRECURSOR (BMP-7) (OSTEOGENIC PROTEIN 1)
DE
     (OP1).
     BMP7 OR OP1.
GN
05
     HOMO SAPIENS (HUMAN).
OC
     EUKARYOTA: METAZOA: CHORDATA: VERTEBRATA: TETRAPODA: MAMMALIA:
OC
     EUTHERIA: PRIMATES.
RN
     [1]
     SEQUENCE FROM N.A., AND PARTIAL SEQUENCE.
RP
RC
     TISSUE=PLACENTA;
RM
     90291971
     OEZKAYNAK E., RUEGER D.C., DRIER E.A., CORBETT C., RIDGE R.J.,
RA
RA
     SAMPATH T.K., OPPERMANN H.;
RL
     EMBO J. 9:2085-2093(1990).
RN
     [2]
RP
     SEQUENCE FROM N.A.
RM
     91088608
RA
     CELESTE A.J., IANNAZZI J.A., TAYLOR R.C., HEWICK R.M., ROSEN V.,
RA
     WANG E.A., WOZNEY J.M.;
     PROC. NATL. ACAD. SCI. U.S.A. 87:9843-9847(1990).
RL
CC
     -!- FUNCTION: INDUCES CARTILAGE AND BONE FORMATION. MAY BE THE
CC
         OSTEOINDUCTIVE FACTOR RESPONSIBLE FOR THE PHENOMENON OF
CC
         EPITHELIAL OSTEOGENESIS.
CC
     -!- SUBUNIT: HOMODIMER, DISULFIDE-LINKED.
     -!- SIMILARITY: TO OTHER GROWTH FACTORS OF THE TGF-BETA FAMILY.
CC
DR
     EMBL; X51801; HSOP1.
DR
     EMBL: M60316; HSTGFBD.
DR
     PIR; S10529; S10529.
DR
     PIR: C39263: C39263.
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DR

PROSITE; PS00250; TGF BETA.

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FT
     PROPEP
                 30
                      292
                               POTENTIAL.
                293
                               BONE MORPHOGENETIC PROTEIN 7.
FT
                      431
     CHAIN
                330
                      396
FT
     DISULFID
                               BY SIMILARITY.
FT
     DISULFID
                359
                      428
                               BY SIMILARITY.
FT
     DISULFID
                363
                      430
                               BY SIMILARITY.
                               INTERCHAIN (BY SIMILARITY).
                395
                      395
FT
     DISULFID
FT
     CARBOHYD
                187
                      187
                               POTENTIAL.
                302
                      302
                               POTENTIAL.
FT
     CARBOHYD
FT
     CARBOHYD
                321
                      321
                               POTENTIAL.
SQ
               431 AA; 49313 MW; 936534 CN;
     SEQUENCE
                                            158 Significance = 54.74
Initial Score
                   132 Optimized Score =
                   56% Matches
                                            161 Mismatches
Residue Identity =
                    11 Conservative Substitutions
Gaps
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                                                                 210
 140
          150
                   160
                            170
                                     180
                                              190
                                                        200
                            90
                                    100
                                             110
                                                      120
                  80
   DLQTLRAGDEGWLVLDVTAASDCWLLKRHKDLGLRLYVETEDGHSVDPGLAGLLGQRAPRSQQPFVVTFFRA
     DSRTLWASEEGWLVFDITATSNHWVVNPRHNLGLQLSVETLDGQSINPKLAGLIGRHGPQNKQPFMVAFFKA
        220
                  230
                           240
                                    250
                                             260
                                                      270
                                                         190
       140
                150
                             160
                                      170
                                               180
                                                                  200
   SPSPIRTPRAVRPLRRRQ----PKKSNELPQANRLPGIFDDVHGSHGRQVCRRHELYVSFQDLGWLDWVIA
                                            1 11 1 111111 1111 11 11
                 1 1
                        11
                            1 11
   TEVHFRSIRSTGSKQRSQNRSKTPKNQEALRMAN-----VAENSSSDQRQACKKHELYVSFRDLGWQDWIIA
       290
                300
                         310
                                      320
                                               330
                                                         340
                                    240
                                              250
                                                       260
         210
                  220
                            230
   PQGYSAYYCEGECSFPLDSCMNATNHAILQSLVHLMKPNAVPKACCAPTKLSATSVLYYDSSNNVILRKHRN
   PEGYAAYYCEGECAFPLNSYMNATNHAIVQTLVHFINPETVPKPCCAPTQLNAISVLYFDDSSNVILKKYRN
                  370
                                     390
                                              400
                                                       410
                                                                420
         360
                            380
          Χ
   MVVKACGCH
   111 11111
   MVVRACGCH
        430
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2. US-07-800-364A-14 (1-281)
BMP7\_MOUSE BONE MORPHOGENETIC PROTEIN 7 PRECURSOR (BMP-7) (OS

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STANDARD:
                                    PRT:
                                           430 AA.
 ID
      BMP7_MOUSE
 AC
      P23359;
      @1-NOV-1991 (REL. 20, CREATED)
 DT
 DT
      01-NOV-1991 (REL. 20, LAST SEQUENCE UPDATE)
 DT
      @1-AUG-1992 (REL. 23, LAST ANNOTATION UPDATE)
      BONE MORPHOGENETIC PROTEIN 7 PRECURSOR (BMP-7) (OSTEOGENIC PROTEIN 1)
 DE
 DE
      (OP1).
 GN
      BMP7 OR OP1.
 05
      MUS MUSCULUS (MOUSE).
      EUKARYOTA; METAZOA; CHORDATA; VERTEBRATA; TETRAPODA; MAMMALIA;
 OC
 OC
      EUTHERIA: RODENTIA.
 RN
      [1]
 RP
      SEQUENCE FROM N.A.
      91354237
 RM
 RA
      OEZKAYNAK E., SCHNEGELSBERG P.N.J., OPPERMANN H.;
 RL
      BIOCHEM. BIOPHYS. RES. COMMUN. 179:116-123(1991).
 CC
      -!- FUNCTION: INDUCES CARTILAGE AND BONE FORMATION. MAY BE THE
 CC
          OSTEOINDUCTIVE FACTOR RESPONSIBLE FOR THE PHENOMENON OF
 CC
          EPITHELIAL OSTEOGENESIS.
 CC
      -!- SUBUNIT: HOMODIMER, DISULFIDE-LINKED.
      -!- SIMILARITY: TO OTHER GROWTH FACTORS OF THE TGF-BETA FAMILY.
 CC
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     EMBL; X56906; MMOP1G.
 DR
      PIR; JQ1184; JQ1184.
 DR
      PROSITE; PS00250; TGF_BETA.
 KW
      SIGNAL; GROWTH FACTOR; CYTOKINE; BONE; CARTILAGE; GLYCOPROTEIN.
 FT
     SIGNAL
                   1
                          29
                                   POTENTIAL.
 FT
     PROPER
                   30
                         291
                                   POTENTIAL.
 FT
                  292
                         430
                                   BONE MORPHOGENETIC PROTEIN 7.
     CHAIN
 FT
     DISULFID
                  329
                         395
                                   BY SIMILARITY.
 FT
     DISULFID
                  358
                         427
                                   BY SIMILARITY.
 FT
     DISULFID
                         429
                  362
                                   BY SIMILARITY.
 FT
     DISULFID
                  394
                         394
                                   INTERCHAIN (BY SIMILARITY).
 FT
                  186
     CARBOHYD
                        186
                                   POTENTIAL.
 FT
                  301
     CARBOHYD
                         301
                                   POTENTIAL.
 FT
                  320
     CARBOHYD
                         320
                                   POTENTIAL.
FT
                  371
      CARBOHYD
                         371
                                   POTENTIAL.
 SQ
     SEQUENCE
                .430 AA; 49283 MW; 934349 CN;
Initial Score
                      132 Optimized Score =
                                                 155 Significance = 53.32
Residue Identity =
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                                            =
                                                 158 Mismatches
                                                                   =
                                                                       118
Gaps
                      11 Conservative Substitutions
                      10
                                20
                                                               50
                                           30
                                                     401
              EPHWKEFRFDLTQIPAGEAVTAAEFRIYK-VPSIHLLNRTLHVSMFQVVQEQSNRESDLFFL
                  1 1
                                                            11 11 1 111111
   VEHDKEFFHPRYHHREFRFDLSKIPEGERVTAAEFRIYKDYIRERFDNETFQITVYQVLQEHSGRESDLFLL
   140
             150
                       160
                                 170
                                           180
                                                     190
                                                               200
                                                                         210
           70
                               90
                                        100
                                                  110
                                                            120
                                                                      130
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1 1 1 11111 1 11 1
                               111 1 11 1
   DSRTIWASEEGWLVFDITATSNHWVVNPRHNLGLQLSVETLDGQSINPKLAGLIGRHGPQNKQPFMVAFFKA
          220
                   230
                             240
                                      250
                                               260
                                                         270
                                                                  280
       140
                 150
                               160
                                        170
                                                  180
                                                           190
                                                                    200
   SPSPIRTPRAVRPLRRRQ----PKKSNELPQANRLPGIFDDVHGSHGRQVCRRHELYVSFQDLGWLDWVIA
                 1 1
                         11
                              1 1
                                             TEVHLRSI RSTGGKQRSQNRSKTPKNQEALRMA----SVAENSSSDQRQACKKHELYVSFRDLGWQDWI IA
        290
                  300
                           310
                                         320
                                                  330
                                                            340
          210
                   220
                             230
                                      240
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                                                         260
                                                                  270
   PQGYSAYYCEGECSFPLDSCMNATNHAILQSLVHLMKPNAVPKACCAPTKLSATSVLYYDSSNNVILRKHRN
   PEGYAAYYCEGECAFPLNSYMNATNHAIVQTLVHFINPDTVPKPCCAPTQLNAISVLYFDDSSNVILKKYRN
                    370
                              380
                                       390
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  350
           360
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                                                                   420
           χ
   MVVKACGCH
   111 11111
   MVVRACGCH
         430
3. US-07-800-364A-14 (1-281)
             BONE MORPHOGENETIC PROTEIN 5 PRECURSOR (BMP-5).
  BMP5 HUMAN
     BMP5 HUMAN
 ID
                   STANDARD:
                                 PRT:
                                        454 AA.
AC
     P22003:
     01-AUG-1991 (REL. 19, CREATED)
DT
     01-AUG-1991 (REL. 19, LAST SEQUENCE UPDATE)
 DT
DT
     01-AUG-1992 (REL. 23, LAST ANNOTATION UPDATE)
DE
     BONE MORPHOGENETIC PROTEIN 5 PRECURSOR (BMP-5).
05
     HOMO SAPIENS (HUMAN).
00
     EUKARYOTA; METAZOA; CHORDATA; VERTEBRATA; TETRAPODA; MAMMALIA;
OC
     EUTHERIA: PRIMATES.
 RN
     [1]
 RP
     SEQUENCE FROM N.A.
 RC
     TISSUE=BONE;
 RM
     91088608
 RA
     CELESTE A.J., IANNAZZI J.A., TAYLOR R.C., HEWICK R.M., ROSEN V.,
     WANG E.A., WOZNEY J.M.;
 RA
     PROC. NATL. ACAD. SCI. U.S.A. 87:9843-9847(1990).
 RL
     -!- FUNCTION: INDUCES CARTILAGE AND BONE FORMATION.
CC
CC
     -!- SIMILARITY: TO OTHER GROWTH FACTORS OF THE TGF-BETA FAMILY.
 DR
     EMBL; M60314; HSTGFBB.
DR
     PIR; A39263; A39263.
DR
     PROSITE; PS00250; TGF BETA.
KW
     SIGNAL; GROWTH FACTOR; CYTOKINE; BONE; CARTILAGE; GLYCOPROTEIN.
FT
     SIGNAL
                  1
                         ?
                                POTENTIAL.
FT
     PROPER
                  ?
                       322
                                POTENTIAL.
```

```
323
                      454
                               BONE MORPHOGENETIC PROTEIN 5.
FT
     CHAIN
                      419
     DISULFID
                353
                               BY SIMILARITY.
FT
FT
     DISULFID
                382
                      451
                               BY SIMILARITY.
FT
     DISULFID
                386
                      453
                               BY SIMILARITY.
                418
                               INTERCHAIN (BY SIMILARITY).
FT
     DISULFID
                      418
     CARBOHYD
                211
                      211
                               POTENTIAL.
FT
                327
                      327
                               POTENTIAL.
FT
     CARBOHYD
FT
     CARBOHYD
                345
                      345
                               POTENTIAL.
                395
                      395
                               POTENTIAL.
FT
     CARBOHYD
SQ
     SEQUENCE
               454 AA; 51736 MW; 1034006 CN;
                   111 Optimized Score =
                                            153 Significance = 52.36
Initial Score
               =
Residue Identity =
                   54% Matches
                                       =
                                            155 Mismatches
                                                            =
                                                                125
                     2 Conservative Substitutions
                                                                  Ü
Gaps
                                                40
                                                         50
                                                                  60
                    10
                             20
                                      30
            EPHWKEFRFDLTQIPAGEAVTAAEFRIYKVPS-IHLLNRTLHVSMFQVVQEQSNRESDLFFL
              VERDKDFSHQRRHYKEFRFDLTQIPHGEAVTAAEFRIYKDRSNNRFENETIKISIYQIIKEYTNRDADLFLL
              180
                         190
                                  200
                                           210
                                                    220
                                                             230
       170
           X
          70
                  80
                           90
                                    100
                                             110
                                                      120
   DLQTLRAGDEGWLVLDVTAASDCWLLKRHKDLGLRLYVETEDGHSVDPGLAGLLGQRAPRSQQPFVVTFFRA
                               1 1 1111 1 1 1 1
                                                 111 1
                                                       1 1 111 1 11 1
   DTRKAQALDVGWLVFDITVTSNHWVINPQNNLGLQLCAETGDGRSINVKSAGLVGRQGPQSKQPFMVAFFKA
                                270
                                         280
                                                  290
                                                           300
     240
              250
                       260
                                  170
                                           180
                                                    190
                                                             200
       140
                150
                         160
   SPSP I RTPRAVRPLRRRQPKKSNELPQANRLPG I FDDVHGSHGRQVCRRHELYVSFQDLGWLDWV I APQGYS
                                           1 1
                          - 1
                                   1
                                      1
   SEVLLRSVRA-ANKRKNQNRNKSSSHQDSSRMSSVGDYNTSEQKQACKKHELYVSFRDLGWQDWIIAPEGYA
             320
                      330
                               340
                                        350
                                                 360
                                                           370
   310
                                         250
              220
                       230
                                240
                                                  260
                                                           270
     210
   AYYCEGECSFPLDSCMNATNHAILQSLVHLMKPNAVPKACCAPTKLSATSVLYYDSSNNVILRKHRNMVVKA
   AFYCDGECSFPLNAHMNATNHAIVQTLVHLMFPDHVPKPCCAPTKLNAISVLYFDDSSNVILKKYRNMVVRS
           390
                    400
                             410
                                       420
                                                430
                                                         440
                                                                  450
  380
   280
   CGCH
   1111
   CGCH
```

Χ

(Item 1 from file: 351) 008644667 WPI Acc No: 91-148697/20

XRAM Acc No: C91-064306

Osteogenic device for implantation in a mammal - comprising a matrix of treated collagen particles and a protein which induces bone formation Patent Assignee: (CREA-) CREATIVE BIOMOLECULES INC; (CREA-) CREATIVE

BIOMOLECUL

Author (Inventor): OPPERMAN H; KUBERASAMP T; RUEGER D C; OZKAYNAK E; PANG R H L

Number of Patents: 005 Number of Countries: 017

Patent Family:

| CC | Number  | Kind | Date   | Week |         |
|----|---------|------|--------|------|---------|
| WO | 9105802 | A    | 910502 | 9120 | (Basic) |
| CA | 2027259 | A    | 910418 | 9126 |         |
| AU | 9066481 | A    | 910615 | 9133 |         |
| EP | 448704  | A    | 911002 | 9140 |         |
| JP | 4502336 | W    | 920423 | 9223 |         |

Priority Data (CC No Date): US 422699 (891017); US 483913 (900222); US 569920 (900820)

Applications (CC, No, Date): JP 90515578 (901015); WO 90US5903 (901015); EP 90916655 (901015)

Language: English

EP and/or WO Cited Patents: EP 128041; EP 148155; EP 169001; EP 169016; EP 182483; EP 212474; EP 230647; EP 309241; US 4172128; US 4294753; US 4394370; US 4434094; US 4563350; US 4563489; US 4657548; US 4703108; US 4725671; US 4789663; US 4812120; US 4824939; US 4837285; US 4894441; WO 8600526; WO 8800205; WO 8909605; WO 8910409; 11Jnl.Ref

Designated States

(National): AU; CA; JP

(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LU; NL; SE; LI

Filing Details: JP04502336 Based on WO 9105802

Abstract (Basic): WO 9105802

An osteogenic device for implantation in a mammal comprises (a) a biocompatible, in vivo biodegradable matrix of mineral-free, delipidated Type I insol. bone collagen particles, depleted in noncollagenous protein and (b) a protein (I) produced by the expression of recombinant DNA in a mammalian cell, (I) comprising 2 oxidised subunits, the amino acid sequence of each subunit being sufficiently duplicative of the amino acid sequence shown (OP1-16V) such that the dimeric species comprising the subunits has a conformation that is capable of inducing endochondral bone formation in a mammal when disposed within the matrix and implanted in the mammal.

An osteogenic protein expressed from recombinant DNA in a mammalian host cell and capable of inducing endochondral bone formation in a mammal when disposed within a matrix implanted in the mammal, comprises (I). Also claimed are a biocompatible, in vivo biodegradable matrix for implantation in a mammal, an osteogenic protein expressed from recombinant DNA in a mammalian host cell, and a biocompatible, in vivo biodegradable matrix for implantation.

USE/ADVANTAGE - The collagen particles are treated to increase the intraparticle porosity and the surface area of the particles. The matrix obtd. may be combined with osteogenic protein to induce endochondral bone formation reliably and reproducibly in a mammalian body. The osteogenic device can induce at the locus of the implant the full developmental cascade of endochondral bone formation including vascularisation, mineralisation and bone marrow differentiation. (I) විවන විශාවකයට්ට වේරාකාරකට කතාරීරැප්රරාව වාර්වකට එක විවිතවිරාව ඉතාගනවත්ව ත්රීමට කලයි ස්දකය

dependent. @(105pp Dvg. No. 0/13)@ File Segment: CPI Derwent Class: B07; D22; Int Pat Class: A61K-037/02; A61K-037/12; C07K-015/06; C07K-017/02; C09H-001/02; C12N-015/00 Chemical Fragment Codes (M1): +01\* N423 N424 N710 N740 N903 N135 P421 P714 Q233 V752

Chemical Fragment Codes (M6):

\*02\* M903 P421 P714 Q233 R220

```
1. US-07-800-364A-7 (1-199)
  Q15242
               BMP-8 peptide.
 ID
     Q15242 standard; DNA; 199 BP.
AC
     Q15242:
DT
     09-MAR-1992 (first entry)
DE
     BMP-8 peptide.
KW
     Cartilage; wound healing; tissue repair; BMP; ss.
05
     Bos taurus.
FH
                     Location/Qualifiers
     Key
FT
     CDS
                     30..176
FT
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FT
     /label= BMP-8
PN
     W09118098-A.
PD
     28-NOV-1991.
PF
     15-MAY-1991; U03388.
PR
     16-MAY-1990; US-525357.
PR
     15-JAN-1991; US-641204.
PΑ
      (GENE-) GENETICS INST INC.
PΙ
     Hewick RM, Wang JH;
DR
     WPI: 91-369252/50.
DR
     P-PSDB; R15522.
PT
     New BMP-8 protein - useful in inducing cartilage and/or bone
PT
     formation to treat wounds and repair fractures and tissues, e.g.
PT
     burns, incisions and ulcers
PS
     Disclosure; Page 27; 50pp; English.
     Nucleotide 95 is a "T" whereas in the amplified DNA fragment the
CC
     corresp. nucleotide is "C".
CC
     This sequence encodes amino acids 64-112 (C-terminal) of the BMP-8
CC
     sequence given in R15522. BMP-8 peptide fragments were purified from
CC
CC
     ground bovine bone powder. Oligonucleotide probes were designed based
CC
     on these peptides and used to screen bovine genomic libraries to
CC
     isolate DNA sequences encoding BMP-8 proteins.
CC
     Pharmaceutical compsns. contg. BMP-8 can be used to aid bone and/or
CC
     cartilage formation or wound healing and tissue repair. The
CC
     proteins are not very species specific so can be used in domestic
CC
     and farm animals as well as humans.
CC
     See also Q15240-48, R15517 and R15522.
SQ
     Sequence
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                           34 A;
                                    87 C;
                                            52 G;
                                                      26 T;
Initial Score
                     199 Optimized Score =
                                                199 Significance = 14.46
                    100% Matches
                                           =
                                                199 Mismatches
Residue Identity =
                                                                       Ø
Gaps
                       Ø Conservative Substitutions
           10
                     20
                               30
                                         40
                                                   50
                                                             60
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    TGCCCGCTGCCCCCTCCCGCCCCGCCAGGTGCACCTGCTGAAGCCGCACGCGGTCCCCAAGGCGTGCTGCG
   X
           10
                     20
                               30
                                         40
                                                   50
                                                             60
                                                                      70
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80 100 110 120 130 140 90 CGCCCACCAAGCTGAGCGCCACTTCCGTGCTCTACTACGACAGCAGCAACAACGTCATCCTGCGCAAGCACC CGCCCACCAAGCTGAGCGCCACTTCCGTGCTCTACTACGACAGCAGCAACAACGTCATCCTGCGCAAGCACC 120 130 80 90 100 110 140 150 160 170 180 190 GCAACATGGTGGTCCGCGCCTGCGGCTGCCACTGAGGCCCCAACTCCACCGGCAG GCAACATGGTGGTCCGCGCCTGCGGCTGCCACTGAGGCCCCAACTCCACCGGCAG 150 160 170 180 190

. US-07-800-364A-7 (1-199)

DRO60APRO D. melanogaster 60A protein (60A) mRNA, complete cd

LOCUS DR060APRO 1632 bp ss-mRNA INV 11-SEP-1992

DEFINITION D. melanogaster 60A protein (60A) mRNA, complete cds.

ACCESSION M84795

KEYWORDS 60A protein; bone morphogenetic protein;

transforming growth factor.

SOURCE Drosophila melanogaster (library: Kopczynski-Muskavitch) embryo

cDNA to mRNA.

ORGANISM Drosophila melanogaster

Eukaryota; Animalia; Metazoa; Arthropoda; Uniramia; Insecta;

Pterygota; Neoptera; Holometabola; Diptera; Brachycera; Cyclorrhapha; Schizophora; Drosophiloidea; Drosophilidae.

REFERENCE 1 (bases 1 to 1632)

AUTHORS Doctor, J.S., Jackson, P.D., Rashka, K.E., Visalli, M. and

Hoffmann, F.M.

TITLE Sequence, biochemical characterization and developmental

expression

of a new member of the TGF-beta superfamily in Drosophila

melanogaster

JOURNAL Dev. Biol. 151, 491-505 (1992)

STANDARD full automatic

FEATURES Location/Qualifiers

CDS 142..1509 /gene="60A"

/product="60A protein"

/codon start=1

/translation="MSGLRNTSEAVAVLASLGLGMVLLMFVATTPPAVEATQSGIYID

NGKDQTIMHRVLSEDDKLDVSYEILEFLGIAERPTHLSSHQLSLRKSAPKFLLDVYHR

ITAEEGLSDQDEDDDYERGHRSRRSADLEEDEGEQQKNF ITDLDKRA I DESD I IMTFL

NKRHHNVDELRHEHGRRLWFDVSNVPNDNYLVMAELRIYQNANEGKWLTANREFTITV

```
YAIGTGTLGQHTMEPLSSVNTTGDYVGWLELNVTEGLHEWLVKSKDNHGIYIGAHAVN
RPDREVKLDDIGLIHRKVDDEFQPFMIGFFRGPELIKATAHSSHHRSKRSASHPRKRK
KSVSPNNVPLLEPMESTRSCQMQTLYIDFKDLGWHDWIIAPEGYGAFYCSGECNFPLN
AHMNATNHA I VQTL VHLLEPKK VPKPCCAPTRLGALP VLYHLNDEN VNLKKYRNM I VK
                   SCGCH"
               414 a
BASE COUNT
                       479 c
                               453 a
                                       286 t
           chromosome 2R--60A
ORIGIN
Initial Score
                   104 Optimized Score =
                                           123 Significance = 6.66
               =
                   63% Matches
                                            134 Mismatches
                                                                62
Residue Identity =
                   16 Conservative Substitutions
Gaps
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              1240
                       1250
                                1260
                                         1270
                                                  1280
                                                           1290
                                     10
                                                  20
                                                           30
                            TGCCGC--TGCCCCCTCC---CG-CCCCGCCAGGTGCACCTG
                                     1 11 1 1
                                                11 11
                                                        11 111 11111
                             11 111
   GAGTGCAATTTCCCGCTCAATGCGCACATGAACGCCACGAACCATGCGATCGTCCAGACCCTGGTCCACCTG
   1300
            1310
                     1320
                            X 1330
                                       1340
                                                1350
                                                         1360
                              70
                                                         100
                                       80
                                                90
   40
            50
                     60
   CTGAAGCCGCACGCGCTCCCCAAGGCGTGCTGCGCGCCCACCAAGCTGAGCGCCACT-TCCGTGCTCTACTA
                CTGGAGCCGAAGAAGGTGCCCAAGCCCTGCTGCGCTCCGACCAGGCTGGGAG-CACTACCCGTTCTGTACCA
  1370
          1380
                   1390
                            1400
                                     1410
                                               1420
                                                        1430
  110
                                                        170
          120
                   130
                            140
                                     150
                                              160
                                                                180
   CGACAGCAGCAACACGTCATCCTGCGCAAGCACCGCAACATGGTGGTCCGCGCCTGCGGCTGCCACTGAGG
          1 1 11 11 1 1111
                            111 1 1 111111 1 11
                                                   CCTGAACGACGAGAATGTGAACCTGAAAAAGTATAGAAACATGATTGTGAAATCCTGCGGGTGCCATTGA--
                                             1490
 1440
          1450
                   1460
                            1470
                                    1480
                                                       1500
          190
   CCCCAACT--CCAC--CGGC--AG
      111 1 1111
                  111
   1510
          1520
                   1530 X
                            1540
                                     1550
                                              1560
                                                       1570
                                                                1580
   TACTARTCTCGARTATTTTTATACARAGATATACAGCGCTGTACCTAACTG
                                   1620
                                            1630
        1590
                 1600
                          1610
1. US-07-800-364A-7 (1-199)
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QQBE8

BPLF1 protein - Human herpesvirus 4 (strain B95-8)

```
QQBE8
                            #Type Protein
ENTRY
 TITLE
                 BPLF1 protein - Human herpesvirus 4 (strain B95-8)
                 25-Feb-1985 #Sequence 25-Feb-1985 #Text 31-Mar-1992
 DATE
PLACEMENT
                 1934.0
                           1.0
                                  1.0
                                         1.0
                                                1.0
SOURCE
                 human herpesvirus 4, Epstein-Barr virus
                 A@3747
ACCESSION
 REFERENCE
                 (Protein coding region)
   #Authors
                 Baer R., Bankier A.T., Biggin M.D., Deininger P.L.,
                   Farrell P.J., Gibson T.J., Hatfull G., Hudson
                   G.S., Satchwell S.C., Seguin C., Tuffnell P.S.,
                   Barrell B.G.
   #Journal
                 Nature (1984) 310:207-211
   #Title
                 DNA sequence and expression of the B95-8
                   Epstein-Barr virus genome.
    #Reference-number A03794
                 The sequence was translated from the DNA sequence,
COMMENT
                   which was obtained from GenBank, release 26.0.
SUMMARY
             #Molecular-weight 337955 #Length 3149 #Checksum 7480
SEQUENCE
Initial Score
                       20 Optimized Score =
                                                      Significance =
                                                  24
Residue Identity =
                      37% Matches
                                                  29 Mismatches
                                                                         35
                       14 Conservative Substitutions
                                                                          0
Translation Frame=
                        1
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     210
               220
                          230
                                    240
                                              250
                                                        260
                                                10
                                                             20
                                                                        30
                                CPLP-----PPAPAR---CTCXSRTRSPRRAARPPSXAPLP
                                 111
                                             11 11
                                                         1
                                                             11 11 1 1 11
   GEAAGTPGADSSPPVMLPFERRIIPYNLRPLPSRSFTSDSFPA-ARYSPAKTNSPPSSPASAA-PASAAPAS
   280
             290
                        300
                                X 310
                                            320
                                                       330
                                                                  340
         40
                    50
                              60
                                     Y
   CSTTTAATTS-SCASTATWWSAPAAATEAPTPPA
               11 1
                         111 1 1 11
   AAPASAAPASAAPASAAPASAAPASAAPASSPPLF I P I PGLGHTPG V PAPSTPPRASSGAAPQTPK RKKGLG
    350
              360
                        370
                                  380
                                            390
                                                      400
   KDSPHKKPTSGRRLPLSSTTDTEDDQLPRTHVPPHRPPSAARLPPPVIPIPHQSPPASPTPH
  420
            430
                      440
                                450
                                                    470
                                                              480
                                          460
```

1. US-07-800-364A-7 (1-199)

TEGU\_EBV LARGE TEGUMENT PROTEIN.

```
ID
      TEGU EBV
                     STANDARD:
                                   PRT: 3149 AA.
 AC
      P03186;
 DT
      21-JUL-1986 (REL. 01, CREATED)
      21-JUL-1986 (REL. Ø1, LAST SEQUENCE UPDATE)
 DT
      01-MAY-1992 (REL. 22, LAST ANNOTATION UPDATE)
 DT
 DE
      LARGE TEGUMENT PROTEIN.
 GN
      BPLF1.
 05
      EPSTEIN-BARR VIRUS (STRAIN B95-8).
 OC
      VIRIDAE; DS-DNA ENVELOPED VIRUSES; HERPESVIRIDAE.
 RN
 RP
      SEQUENCE FROM N.A.
 RM
      84270667
      BAER R., BANKIER A.T., BIGGIN M.D., DEININGER P.L., FARRELL P.J.,
 RA
      GIBSON T.J., HATFULL G., HUDSON G.S., SATCHWELL S.C., SEGUIN C.,
 RA
     TUFFNELL P.S., BARRELL B.G.;
 RA
     NATURE 310:207-211(1984).
 RL
 CC
      -!- FUNCTION: TEGUMENT PROTEIN.
 CC
      -!- SIMILARITY: BELONGS TO FAMILY THAT GROUPS TOGETHER HSV-1 UL36,
 CC
          EBV BPLF1, AND VZV 22.
 DR
      EMBL: VØ1555; EBV.
 DR
      PIR; A03747; QQBE8.
 SQ
      SEQUENCE
                3149 AA; 337954 MW; 1.650784E+07 CN;
                      20 Optimized Score =
                                                 24 Significance = 5.70
Initial Score
                 =
                      37% Matches
                                                 29 Mismatches
Residue Identity =
                                                                       35
                       14 Conservative Substitutions
                                                                        Ø
Translation Frame=
    AHVRVSTYAHDILQYVGAPGAQYTCVHLYFLPEAFETEDPRIFMLEHYGVYDFYEANGSGFDLVGPELVSSD
      210
                220
                         230
                                   240
                                             250
                                                       260
                                                                 270
                                Χ
                                               10
                                                            20
                                                                      30
                                CPLP----PPAPAR---CTCXSRTRSPRRAARPPSXAPLP
                                111
                                            11 11
                                                        GEAAGTPGADSSPPVMLPFERRI IPYNLRPLPSRSFTSDSFPA-ARYSPAKTNSPPSSPASAA-PASAAPAS
    280
             290
                        300
                               X 310
                                           320
                                                      330
                                                                 340
         40
                    50
                             60
    CSTTTAATTS-SCASTATWWSAPAAATEAPTPPA
         11 1 11 1
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    350
              360
                        370
                                 380
                                           390
                                                     400
                                                               410
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  420
            430
                      440
                               450
                                         460
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                                                             480
2. US-07-800-364A-7 (1-199)
```

HYPOTHETICAL PROTEIN E-115.

Y115 ADE02

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PRT: 115 AA.
     Y115 ADE02
                   STANDARD:
 ID
AC
     P03290:
     21-JUL-1986 (REL. 01, CREATED)
DT
     21-JUL-1986 (REL. 01, LAST SEQUENCE UPDATE)
DT
     @1-APR-199@ (REL. 14, LAST ANNOTATION UPDATE)
DT
     HYPOTHETICAL PROTEIN E-115.
DE
05
     HUMAN ADENOVIRUS TYPE 2.
OC
     VIRIDAE; DS-DNA NONENVELOPED VIRUSES; ADENOVIRIDAE.
RN
RP
     SEQUENCE FROM N.A.
RM
     83056843
RA
     GINGERAS T.R., SCIAKY D., GELINAS R.E., BING-DONG J., YEN C.E.,
     KELLY M.M., BULLOCK P.A., PARSONS B.L., O'NEILL K.E., ROBERTS R.J.;
RA
RL
     J. BIOL. CHEM. 257:13475-13491(1982).
DR
     EMBL; J01917; AD2.
     PIR; A03862; A03862.
DR
KW
     HYPOTHETICAL PROTEIN.
SQ
     SEQUENCE 115 AA; 12236 MW; 68893 CN;
                                            23 Significance = 5.18
Initial Score =
                    12 Optimized Score =
                                             26 Mismatches =
                    29% Matches
Residue Identity =
                                       =
                   21 Conservative Substitutions
                                                                   Ø
Translation Frame=
                                                20
                                                          30
                            10
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                      MGETWFLTPNGQSSPGSWNARPSAGPAARMPTPRNRYFSRPSSTPLKVCTAPRAAPPPRASCAPRATPRRGW
           10
                    20
                             30
                                      40 50 60
                            60
          50
   TSSCASTATW-----WSAPA-AATEAPTPPA
                      TMTPWSNATWPTRRAKTGSASAPAGPASSAPWPARSPERTPSP
1. US-07-800-364A-9 (1-172)
  A33532 *Mucin - Human (fragment)
ENTRY
                         #Type Protein (fragment)
               A33532
               *Mucin - Human (fragment)
TITLE
DATE
               04-Sep-1992 #Sequence 04-Sep-1992 #Text 04-Sep-1992
PLACEMENT
                  0.0
                        0.0
                               0.0
                                     0.0
                                            0.0
               *This entry is not verified.
COMMENT
SOURCE
               Homo sapiens #Common-name man
REFERENCE
               Gum J.R., Byrd J.C., Hicks J.W., Toribara N.W.,
   #Authors
                Lamport D.T.A., Kim Y.S.
               J. Biol. Chem. (1989) 264:6480-6487
   #Journal
```

#Title Molecular cloning of human intestinal mucin cDNAs. Sequence analysis and evidence for genetic polymorphism. #Reference-number A33532 A33532 #Accession #Cross-reference GB:M22404; GB:M22405; GB:M22406 SUMMARY #Length 519 #Checksum 4853 SEQUENCE Initial Score 11 Optimized Score = 23 Significance = 7.3633% Matches 26 Mismatches 31 Residue Identity = 20 Conservative Substitutions 0 Translation Frame= 1 1. US-07-800-364A-11 (1-119) 516244 Bone morphogenetic protein 2 precursor - African **ENTRY** #Type Protein TITLE Bone morphogenetic protein 2 precursor - African clawed from DATE 30-Jun-1992 #Sequence 30-Jun-1992 #Text 31-Sep-1992 **PLACEMENT** 0.0 0.0 0.0 0.0 0.0 Xenopus laevis #Common-name African clawed frog SOURCE S16244 ACCESSION REFERENCE Plessow S., Koester M., Knoechel W. #Authors Biochim. Biophys. Acta (1991) 1089:280-282 #Journal #Title cDNA sequence of Xenopus laevis bone morphogenetic protein 2 (BMP-2). #Reference-number S16244 #Accession S16244 #Molecule-type mRNA #Residues 1-398 (PLE) #Cross-reference EMBL:X55031 KEYWORDS dimer\ glycoprotein FEATURE 285-398 #Protein bone morphogenetic protein 2 (predicted) (MAT)\ 137, 202, 340 #Binding-site carbohydrate (Asn) (covalent) (predicted) #Molecular-weight 45575 #Length 398 #Checksum 9714 SUMMARY SEQUENCE Initial Score 11 Optimized Score = 15 Significance = 6.02 32% Matches 18 Mismatches Residue Identity = 21 = 16 Conservative Substitutions 0

Translation Frame=

1

| SDSSKLHRINI<br>170            | YDIVKPAAAAS<br>180 |  |                         | FDVTPAIARWI<br>10 22 | AHKQPNHGFVVEVNHLD<br>Ø 230   |
|-------------------------------|--------------------|--|-------------------------|----------------------|------------------------------|
|                               |                    | X<br>PLRVPA<br>I                               | 10<br>DDVHGSHG<br>I I I |                      | 20<br>VCRRHELYVSFQ<br>       |
|                               |                    | NWPQIRPLLVTFS<br>260 X 270                     |                         |                      | KRLKSSCRRHPLYVDFS<br>300     |
| 30 X<br>DLGWLVSSDSP<br>I II I |                    |  |                         |                      |                              |
| DVGWNDWIVAP<br>310 32         |                    |  | NHAIVQTLVN<br>350       | SVNTNIPKACC<br>360   | VPTELSAISMLYLDENE<br>370 380 |
| KVVLKNYQDMV<br>390            | VEGCGCR            |  |                         |                      |                              |
| 2. US-07-800-36<br>B39263     |                    | (9)<br>phogenetic pr                           | otein 6 -               | Human                |                              |
| ENTRY                         | B39263             | #Type Prot                                     | ein                     |                      |                              |
| TITLE                         |                    | phogenetic p                                   | rotein 6 -              |                      |                              |
| DATE                          | 04-Oct-19          | 91 #Sequence                                   | 04-Oct-19               | 91 #Text 04          | -Oct-1991                    |
| PLACEMENT                     | 0.0                | 0.0 0.0  | 0.0                     | 0.0                  |                              |
| COMMENT                       | *This ent          | ry is not ve                                   | rified.                 |                      |                              |
| SOURCE<br>REFERENCE           | ·                  | ens #Common-                                   |                         |                      |                              |
| #Authors                      | R.M., F            | A.J., Iannazz<br>Rosen V., Wan                 | g E.A., Wo              | zney J.M.            |                              |
| #Journal<br>#Title            |                    | l. Acad. Sci                                   |                         |                      |                              |
| #11616                        | family             | eation of tra<br>members pres<br>ed from bovin | ent in bon              |                      |                              |
| #Reference-                   |                    |  |                         |                      |                              |
| #Accession                    | B39263             |  |                         |                      |                              |
| #Cross-refe                   | rence GB:M3        | 88694  |                         |                      |                              |
| SUMMARY<br>SEQUENCE           | #Molecular-        | weight 57225                                   | #Length                 | 513 #Check           | sum 183                      |
| Initial Score                 | = 14               | Optimized S                                    | core =                  | 19 Signi             | ficance = 10.04              |
| Residue Identit               | y = 50%            | Matches  | =                       | 20 Misma             | tches = 19                   |
| Gaps                          | = 1                | Conservativ                                    | e Substitu              | tions                | = 0                          |
| Translation Fra               | me= 1              |  |                         |                      |                              |
| TOURNETER                     | LH CENTTATAL       | II LIIHITOODAMOLA                              | יים מווודם אריי         | אווטמטטטפי ייכ       | DUCUALA                      |
| 300<br>300                    | 310                |  |                         |                      | RDGPYDKQPFMVAFFKV<br>50 360  |
|                               |                    | X  | 10                      | 20                   | 30 X                         |

```
PLRV-PADDVHGSHGRQVCRRHELYVSFQDLGWLVSSDSP
                                 SEVHVRTTRSASSRRRQQSRNRSTQSQDVARVSSASDYNSSELKTACRKHELYVSFQDLGWQDWI IAPKGYA
                                                                 430 X
     370
               380
                         390
                               Х
                                   400
                                             410
                                                       420
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                                           480
                                                     490
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                       460
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 510
3. US-07-800-364A-11 (1-119)
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               Osteogenic protein 1 precursor - Mouse
ENTRY
                JQ1184
                           #Type Protein
TITLE
                Osteogenic protein 1 precursor - Mouse
DATE
                31-Dec-1991 #Sequence 31-Dec-1991 #Text 31-Sep-1992
PLACEMENT
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                                        0.0
                                               0.0
                Mus musculus #Common-name house mouse
SOURCE
ACCESSION
                JQ1184\ PQ0224
REFERENCE
   #Authors
                Oezkaynak E., Schnegelsberg P.N.J., Oppermann H.
                Biochem. Biophys. Res. Commun. (1991) 179:116-123
   #Journal
                Murine osteogenic protein (OP-1): high levels of
   #Title
                  mRNA in kidney.
   #Reference-number JQ1184
   #Accession
               JQ1184
   #Molecule-type DNA
   #Residues
                1-120 (OEZ)
   #Cross-reference EMBL: X56906
   #Accession PQ0224
   #Molecule-type mRNA
                54-430 (OE2)
   #Residues
COMMENT
                This protein induces bone formation.
FEATURE
   1-29
                           #Domain signal sequence (SIG)\
   30-290
                           #Peptide propeptide (predicted) (PRO)\
                           #Protein osteogenic protein-1
   291-430
                              (experimental) (MAT)\
                           #Binding-site carbohydrate (Asn)
   186, 301, 320, 371
                              (covalent) (predicted)
              #Molecular-weight 49283 #Length 430 #Checksum 9190
SUMMARY
SEQUENCE
Initial Score
                      14 Optimized Score =
                                                 17 Significance =
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                     45% Matches
                                                 18 Mismatches
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Residue Identity =
                       1 Conservative Substitutions
Translation Frame=
                       1
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           220
                     230
                               240
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                                                             270
                                                                       280
                                                   20
                                                             30
                                                                       Χ
                                X
                                         10
                               PLR-VPADDVHGSHGRQVCRRHELYVSFQDLGWLVSSDSP
                                           1 11 1 1111111 1111
                                11
    TEVHLRS I RSTGGKQRSQNRSKTPKNQEALRMASVAENSSSDQRQACKKHELYVSFRDLGWQDWI I APEGYA
        290
                   300
                             310
                                       320
                                                 330
                                                           340
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                                     390
                                               400
                370
                           380
                                                         410
                                                                   420
   CGCH
    430
4. US-07-800-364A-11 (1-119)
  C39263
               *Bone morphogenetic protein 7 - Human
ENTRY
                 C39263
                            #Type Protein
                 *Bone morphogenetic protein 7 - Human
TITLE
                 04-Oct-1991 #Sequence 04-Oct-1991 #Text 04-Oct-1991
DATE
 PLACEMENT
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COMMENT
                 *This entry is not verified.
SOURCE
                 Homo sapiens #Common-name man
 REFERENCE
                 Celeste A.J., Iannazzi J.A., Taylor R.C., Hewick
   #Authors
                   R.M., Rosen V., Wang E.A., Wozney J.M.
                 Proc. Natl. Acad. Sci. U.S.A. (1990) 87:9843-9847
   #Journal
   #Title
                 Identification of transforming growth factor beta
                   family members present in bone-inductive protein
                   purified from bovine bone.
   #Reference-number A39263
   #Accession
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   #Cross-reference GB:M38695
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                      45% Matches
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                                                                        21
Residue Identity =
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Translation Frame=
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                    230
                              240
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                                                  260
                                                            270
                                                                      280
                                         10
                                                   20
                                                             30
                                                                       X
                                PLR-VPADDVHGSHGRQVCRRHELYVSFQDLGWLVSSDSP
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                                              1
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290 300 310 X 320 330 340 350 AYYCEGECAFPLNSYMNATNHAIVQTLVHFINPETVPKPCCAPTQLNAISVLYFDDSSNVILKKYRNMVVRA 360 370 380 390 400 410 420 CGCH 430 5. US-07-800-364A-11 (1-119) \*Osteogenic protein precursor - Human S10529 ENTRY #Type Protein TITLE \*Osteogenic protein precursor - Human DATE 15-Jun-1992 #Sequence 15-Jun-1992 #Text 15-Jun-1992 PLACEMENT 0.0 0.0 0.0 0.0 COMMENT \*This entry is not verified. SOURCE Homo sapiens #Common-name man REFERENCE Dezkaynak E., Rueger D.C., Drier E.A., Corbett C., #Authors Ridge R.J., Sampath T.K., Oppermann H. #Journal EMBO J. (1990) 9:2085-2093 #Title OP-1 cDNA encodes an osteogenic protein in the TGF-beta family. #Reference-number S10529 S10529 #Accession #Cross-reference EMBL: X51801 #Molecular-weight 49313 #Length 431 #Checksum SUMMARY 128 SEQUENCE Initial Score 8.03 14 Optimized Score = 17 Significance = 45% Matches 21 Residue Identity = 18 Mismatches Gaps 1 Conservative Substitutions 0 Translation Frame= 1 DSRTLWASEEGWLVFDITATSNHWVVNPRHNLGLQLSVETLDGQSINPKLAGLIGRHGPQNKQPFMVAFFKA 220 230 240 250 260 270 280 X 10 20 30 Х PLR-VPADDVHGSHGRQVCRRHELYVSFQDLGWLVSSDSP 1 11 1 111111 1111 11 TEVHFRSIRSTGSKQRSQNRSKTPKNQEALRMANVAENSSSDQRQACKKHELYVSFRDLGWQDWIIAPEGYA 300 290 310 X 320 330 340 AYYCEGECAFPLNSYMNATNHAIVQTLVHFINPETVPKPCCAPTQLNAISVLYFDDSSNVILKKYRNMVVRA 360 370 380 390 400 410 420 CGCH 430

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                *Vg-1-related protein precursor - Mouse
   A33925
 ENTRY
                 A33925
                            #Type Protein
                 *Vg-1-related protein precursor - Mouse
 TITLE
 DATE
                 19-Sep-1992 #Sequence 19-Sep-1992 #Text 19-Sep-1992
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                                                0.0
 COMMENT
                 *This entry is not verified.
 SOURCE
                 Mus musculus #Common-name house mouse
 REFERENCE
    #Authors
                 Lyons K., Graycar J.L., Lee A., Hashmi S., Lindquist
                   P.B., Chen E.Y., Hogan B.L.M., Derynck R.
                 Proc. Natl. Acad. Sci. U.S.A. (1989) 86:4554-4558
    #Journal
    #Title
                 Vgr-1, a mammalian gene related to Xenopus Vg-1, is
                   a member of the transforming growth factor
                   beta-gene superfamily.
    #Reference-number A33925
    #Accession
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    #Cross-reference GB:J04566
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                                                                       8.03
                      43% Matches
                                                   17 Mismatches
                                                                         22
Residue Identity =
                        O Conservative Substitutions
                                                                          0
Translation Frame=
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            230
                      240
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                                          260
                                                     270
                                                               280
                                                                         290
                                                  20
                                                             30
                                                                       X
                                        10
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                                         11
                                                  1 11111111111
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                                                             350
          300
                    310
                              320
                                        330
                                                  340
                                                                       360
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        370
                  380
                            390
                                      400
                                                410
                                                           420
                                                                     430
    GCH
7. US-07-800-364A-11 (1-119)
   A39263
                *Bone morphogenetic protein 5 - Human
 ENTRY
                            #Type Protein
                 A39263
 TITLE
                 *Bone morphogenetic protein 5 - Human
 DATE
                 04-Oct-1991 #Sequence 04-Oct-1991 #Text 04-Oct-1991
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0.0

0.0

0.0

0.0

0.0

PLACEMENT

COMMENT \*This entry is not verified. SOURCE Homo sapiens #Common-name man REFERENCE #Authors Celeste A.J., Iannazzi J.A., Taylor R.C., Hewick R.M., Rosen V., Wang E.A., Wozney J.M. #Journal Proc. Natl. Acad. Sci. U.S.A. (1990) 87:9843-9847 #Title Identification of transforming growth factor beta family members present in bone-inductive protein purified from bovine bone. #Reference-number A39263 A39263 #Accession #Cross-reference GB:M38693 SUMMARY #Molecular-weight 51736 #Length 454 #Checksum 4416 SEQUENCE Initial Score 11 Optimized Score = 16 Significance = 7.03 41% Matches Residue Identity = 16 Mismatches 23 @ Conservative Substitutions 0 Translation Frame= 1 DTRKAQALDVGWLVFDITVTSNHWVINPQNNLGLQLCAETGDGRSINVKSAGLVGRQGPQSKQPFMVAFFKA 270 280 290 300 240 250 260 10 20 30 X PLRVPADDVHGSHGRQVCRRHELYVSFQDLGWLVSSDSP 1 1 111111 1111 SEVLLRSVRAANKRKNONRNKSSSHODSSRMSSVGDYNTSEQKQACKKHELYVSFRDLGWQDWIIAPEGYAA X 340 350 360 370 Χ 310 320 330 FYCDGECSFPLNAHMNATNHAIVQTLVHLMFPDHVPKPCCAPTKLNAISVLYFDDSSNVILKKYRNMVVRSC 440 380 390 400 410 420 430 450 GCH 8. US-07-800-364A-11 (1-119) C39364 \*GDF-1 embryonic growth factor - Human ENTRY C39364 #Type Protein \*GDF-1 embryonic growth factor - Human TITLE DATE 03-Mar-1992 #Sequence 03-Mar-1992 #Text 03-Mar-1992 0.0 0.0 0.0 PLACEMENT 0.0 0.0 \*This entry is not verified. COMMENT SOURCE Homo sapiens #Common-name man REFERENCE Lee S.J. #Authors Proc. Natl. Acad. Sci. U.S.A. (1991) 88:4250-4254 #Journal

Expression of growth/differentiation factor 1 in the nervous system: conservation of a bicistronic

#Title

structure. #Reference-number A39364 #Accession C39364

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 ID
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                                     PRT:
                                            513 AA.
 AC
      P22004:
 DT
      01-AUG-1991 (REL. 19, CREATED)
      01-AUG-1991 (REL. 19, LAST SEQUENCE UPDATE)
 DT
      @1-AUG-1992 (REL. 23, LAST ANNOTATION UPDATE)
 DT
 DE
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 05
      HOMO SAPIENS (HUMAN).
 OC
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      EUTHERIA; PRIMATES.
 RN
      [1]
 RP
      SEQUENCE FROM N.A.
 RC
      TISSUE=BONE;
 RM
      91088608
      CELESTE A.J., IANNAZZI J.A., TAYLOR R.C., HEWICK R.M., ROSEN V.,
 RA
 RA
      WANG E.A., WOZNEY J.M.;
 RL
      PROC. NATL. ACAD. SCI. U.S.A. 87:9843-9847(1990).
 CC
      -!- FUNCTION: INDUCES CARTILAGE AND BONE FORMATION.
      -!- SIMILARITY: TO OTHER GROWTH FACTORS OF THE TGF-BETA FAMILY.
 CC
 DR
      EMBL; M60315; HSTGFBC.
 DR
      PIR; B39263; B39263.
 DR
      PROSITE; PS00250; TGF_BETA.
ΚW
      SIGNAL; GROWTH FACTOR; CYTOKINE; BONE; CARTILAGE; GLYCOPROTEIN.
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      SIGNAL
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                                   POTENTIAL.
 FT
      PROPER
                    ?
                         381
                                   POTENTIAL.
FT
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                         513
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FT
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                  412
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FT
     DISULFID
                         510
                  441
                                   BY SIMILARITY.
FT
      DISULFID
                  445
                         512
                                   BY SIMILARITY.
FT
     DISULFID
                  477
                         477
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 FT
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FT
     CARBOHYD
                  269
                         269
                                   POTENTIAL.
 FT
     CARBOHYD
                  386
                         386
                                   POTENTIAL.
FT
     CARBOHYD
                 404
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FT
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DT
      01-NOV-1991 (REL. 20, LAST SEQUENCE UPDATE)
DT
      @1-AUG-1992 (REL. 23, LAST ANNOTATION UPDATE)
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DΕ
DΕ
      (OP1).
      BMP7 OR OP1.
GN
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OC.
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OC
      EUTHERIA; RODENTIA.
RN
      [1]
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     OEZKAYNAK E., SCHNEGELSBERG P.N.J., OPPERMANN H.;
 RA
 RL
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      -!- SUBUNIT: HOMODIMER, DISULFIDE-LINKED.
CC
      -!- SIMILARITY: TO OTHER GROWTH FACTORS OF THE TGF-BETA FAMILY.
CC
DR
     EMBL; X56906; MMOP1G.
DR
      PIR; JQ1184; JQ1184.
      PROSITE; PS00250; TGF_BETA.
DR
KW
     SIGNAL; GROWTH FACTOR; CYTOKINE; BONE; CARTILAGE; GLYCOPROTEIN.
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FT
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     DISULFID
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FT
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                         427
                                   BY SIMILARITY.
FT
     DISULFID
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FT
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                 394
                         394
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FT
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                        186
                                  POTENTIAL.
FT
     CARBOHYD
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                        301
                                  POTENTIAL.
FT
                 320
                        320
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FT
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                                                  260
                                                            270
                               Χ
                                        10
                                                  20
                                                            30
                                                                      χ
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                                          1 11 1 111111 1111
                               11
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   CGCH
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         (C. BIOSIS 1993)
 **FILE 5: Biosystematic Codes (BC=) for viruses have changed for 1993.
 Type ?NEWS5 for more information and a complete list of the new codes.
  File 399:CA SEARCH 1967-1992 UD=11726
         (COPR. 1993 BY THE AMER. CHEM. SOC.)
 **FILE399: Use is subject to the terms of your user customer agreement.
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                  PHE
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008865227 WPI Acc No: 91-369252/50
XRAM Acc No: C91-159207
    New BMP-8 protein - useful in inducing cartilage and/or bone formation
    to treat wounds and repair fractures and tissues, e.g. burns, incisions
    and ulcers
Patent Assignee: (GENE-) GENETICS INST INC
Author (Inventor): HEWICK R M; WANG J H
Number of Patents: 001
Number of Countries: 014
Patent Family:
    CC Number
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                                    Week
                          Date
    WO 9118098
                 Α
                           911128
                                      9150
                                              (Basic)
Priority Data (CC No Date): US 525357 (900516); US 641204 (910115)
Language: English
EF and/or WO Cited Patents: 1. Jnl. Ref; WO 8910409; WO 9011366
Designated States
 (National): CH; JP
 (Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LU; NL; SE
Abstract (Basic): WO 9118098
         A purified BMP-8 protein is claimed, comprising at least one of
    the following sequences; (a)
    Arg-His-Glu-Leu-Tyr-Val-Ser-Phe-Glu-Asp-Leu-Gly-Trp-Leu-Asp-Trp-Val-Ile
    -Ala-Pro-Glu- Gly-Tyr; (b) Leu-Ser-Ala-Thr-Ser-Val-Leu
    Tyr-Tyr-Asp-Ser-Ser-Asn-Asn-Val-Ile-Leu-Arg; (c)
    Ala-Cys-Cys-Ala-Pro-Thr-Lys; (d) Thr-Asn-Glu-Leu-Pro-Pro-Pro
    Asn-Lys-Leu-Pro-Gly-Ile-Phe-Asp-Asp-Val-His-Gly-Ser- His-Gly-Arg; and
    (e) the sequences homologous to the above sequences. Also claimed are a
    DNA sequence encoding a BMF-8 protein, a host cell transformed with the
    DNA and a method for producing the protein.
          USE/ADVANTAGE - BMP-8 protein induces the formation of cartilage
    and/or bone and is used to heal wounds and repair tissue (claimed), eg
    burns, incisions and ulcers. It is also used to repair fractures and
    other defects or periodontal diseases. @(50pp Dwg.No.0/0)@
File Segment: CPI
Derwent Class: B04; D16;
Int Pat Class: A61K-037/02; C12N-015/12; C12P-021/02
Manual Codes (CPI/A-N): B04-B04A; B04-B04A1; B04-C01; B12-A07; B12-J08;
    B12-L02; B12-L03; D05-C12; D05-H03B; D05-H12
Chemical Fragment Codes (M1):
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            $0.63
                     0.019 Hrs File155
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riducabada

\$0.63

Estimated cost File155

\$1.80 1 Types

 1. <u>5.011,691</u> , Apr. 30, 1991, Osteogenic devices; Hermann Oppermann, et al., 424/423, 426; 514/2, 21; 530/350, 395, 840 [IMAGE AVAILABLE]

US PAT NO: 5,011,691 [IMAGE AVAILABLE] L1: 1 of 1

DATE FILED: Feb. 23, 1989

REL-US-DATA: Continuation-in-part of Ser. No. 232,630, Aug. 15, 1988, which is a continuation-in-part of Ser. No. 179,406,

Apr. 8, 1988, Fat. No. 4,968,590.

### ABSTRACT:

Disclosed are (1) osteogenic devices comprising a matrix containing osteogenic protein and methods of inducing endochondral bone growth in mammals using the devices; (2) amino acid sequence data, amino acid composition, solubility properties, structural features, homologies and various other data characterizing osteogenic proteins, (3) methods of producing osteogenic proteins using recombinant DNA technology, and (4) osteogenically and chondrogTERMINAL (ENTER 1, 2, 3, 4, OR ?):3 \$1691pn=s pn5=01165901

L1 1 PN=5011691

el, abcitd, fcdi, tr, efld, , arb

1. <u>5,011,691</u>, Apr. 30, 1991, Osteogenic devices; Hermann Oppermann, et al., 424/423, 426; 514/2, 21; 530/350, 395, 840 [IMAGE AVAILABLE]

US PAT NO: 5,011,691 [IMAGE AVAILABLE] L1: 1 of 1

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- => s Glus( 2GWl)up(r2oW()2prWo)(h2isW()2hWi)st(r2pW()2tWr)pl(y2sW()2lWy)sg(l2uW( WድpWè)up(h2e
- L2 ( 2966)GLU
- L3 ( 9856)PRO
- L4 ( 107016)HIS
- L5 ( 2510)TRP
- L6 ( 2973)LYS
- L7 ( 2966)GLU
- L8 ( 3474) PHE
- L9 Ø GLU(2W) PRO(2W) HIS (2W) TRP (2W) LYS (2W) GLU (2W) PHE
- =) s alas( 2aW1)ac(y2sW)(c2yWs)c(y2sW()2cWy)sa(12aW()2aW1)ap(r2oW()2pWr)ot(h2rW( W2tWb)r1(y2s
- L10 ( 3842)ALA
- L11 ( 1903)CYS
- L12 ( 1903) CYS
- L13 ( 3842)ALA

```
131
   cgtacatgcc
         ggccgtcaag
                gacggcgagt
                       teggetteaa
                               ccttctggtg
801
   ggegggttea
          <u>tcaqccccaa</u>
                gaggtgggcc
                        gaggegttge
                             egetegaege
851
   etgggtegee
         ggggacgacg
                tegteeeegt
                        gtgcaaggcc
                               atcctcgagg
901
   cgtaccggga. . .
EØGLØG Y
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L15 (
          3202) THR
L16 (
          2973) LYS
             @ ALA(2W)CYS(2W)CYS(2W)ALA(2W)PRO(2W)THR(2W)LYS
L17
=> s thrs( 2tWh)ra(s2nW()2aWs)ng(12uW()2gWl)u1(e2uW()21We)up(r2oW()2pWr)op(r2oW)
Wpaswo)p(r2oW()2pWr)oa(s2n
L18 (
          3202) THR
L19 (
          2046) ASN
L20 (
          2966) GLU
          3565) LEU
L21 (
L22 (
          9856) PRO
L23 (
          9856) PRO
          9856) PRO
L24 (
L25 (
          2046) ASN
             Ø THR (2W) ASN (2W) GLU (2W) LEU (2W) PRO (2W) PRO (2W) PRO (2W) ASN
L26
≢©CG??GAsA T?TGCACAGT?
L27
            23 ?GAATTCCG?
BCCB?L27S ALN2D7
                   ?AANDG C?CACCGAC?
             5) ?AGCCCCA?
L28 (
             1 L27 AND ?AGCCCCA?
L29
EL, DBCITD, FCIDT, , RFELD, , ARB
    4,997,930, Mar. 5, 1991, Cloning of complementary DNA encoding maize
nitrite reductase; Kristine N. Lahners, et al., 536/27; 435/69.1, 70.1,
172.3, 240.4, 317.1, 320.1; 935/18, 21, 35, 64, 78, 79 [IMAGE AVAILABLE]
               4,997,930 [IMAGE AVAILABLE]
                                                         L29: 1 of 1
US PAT NO:
DATE FILED:
               Mar. 16, 1989
ABSTRACT:
Maize cDNA coding for nitrite reductase is cloned, using a spinach
nitrite reductase cDNA as a heterologous probe, and is characterized. A
method is provided to use the cloned maize nitrite reductase cDNA to
determine the number of nitrite reductase genes per maize genome and to
study nitrite reductase mRNA regulation in maize.
=KWDCKWIDC
US PAT NO:
               4,997,930 [IMAGE AVAILABLE]
                                                         L29: 1 of 1
CLAIMS:
CLMS(2)
2. An isolated DNA sequence according to claim 1, wherein the sequence
comprises:
    <u>qaatteeggg</u>
         ccgcacaggg
                egegeeegeg
                        eggeegtete
                               egtgeegeeg
51 ceggeggggg
         agcaggtccc
                gacggagcgg
                        ctggagccga
                               gggtcgagga
101
         tgtacgagca
```

cccgcacatc

aacgacctcg

プンジロナド ハン

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| ☐ LINES OR MARKS ON ORIGINAL DOCUMENT☐ REPERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY   |         | COLORED OR BLACK AND WHITE PHOTOGRAPHS                |
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|  | 0       | LINES OR MARKS ON ORIGINAL DOCUMENT                   |
| OTHER:   | 0       | REPERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY |
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